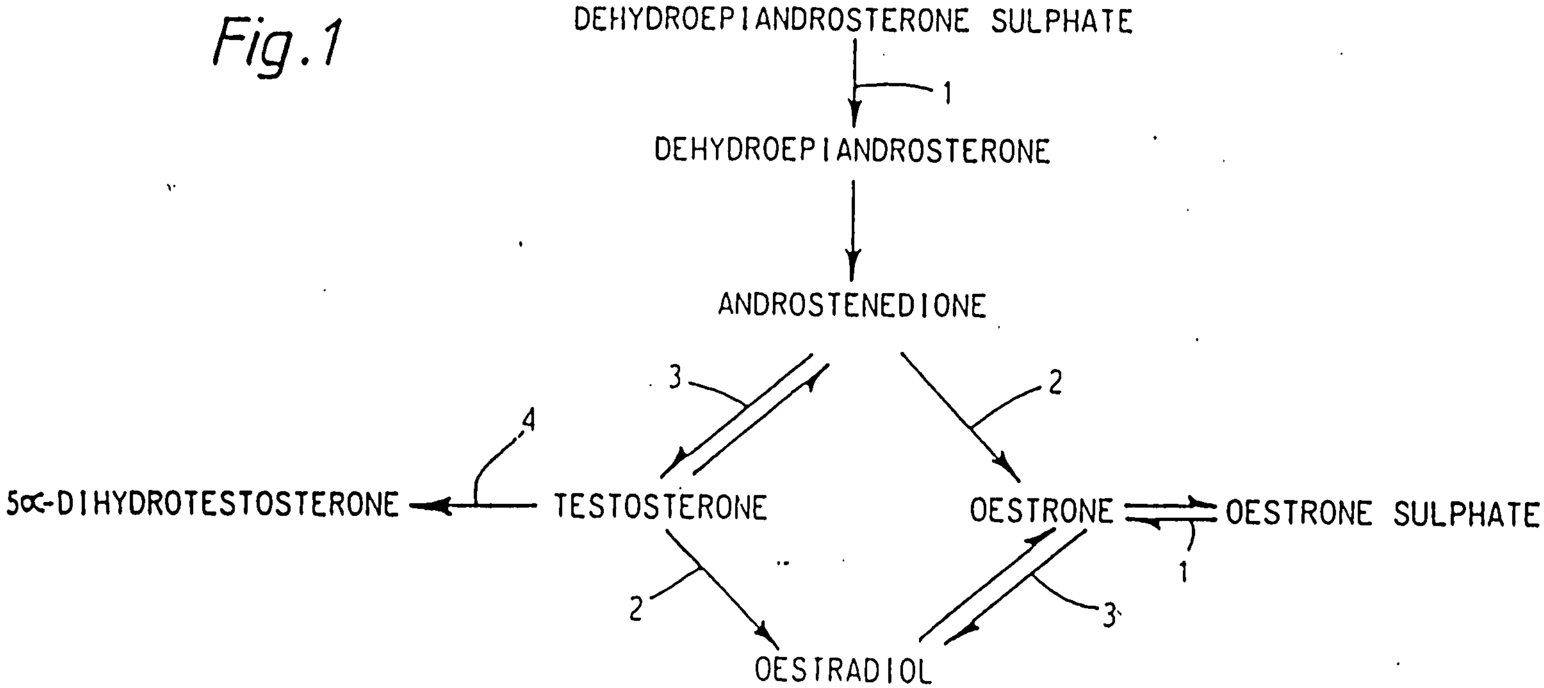
Fig.1



KEY ENZYMES IN STEROIDOGENESIS:-

1. SULPHATASE 2. AROMATASE 3. DEHYDROGENASE 4. 5α REDUCTASE

Fig. 2

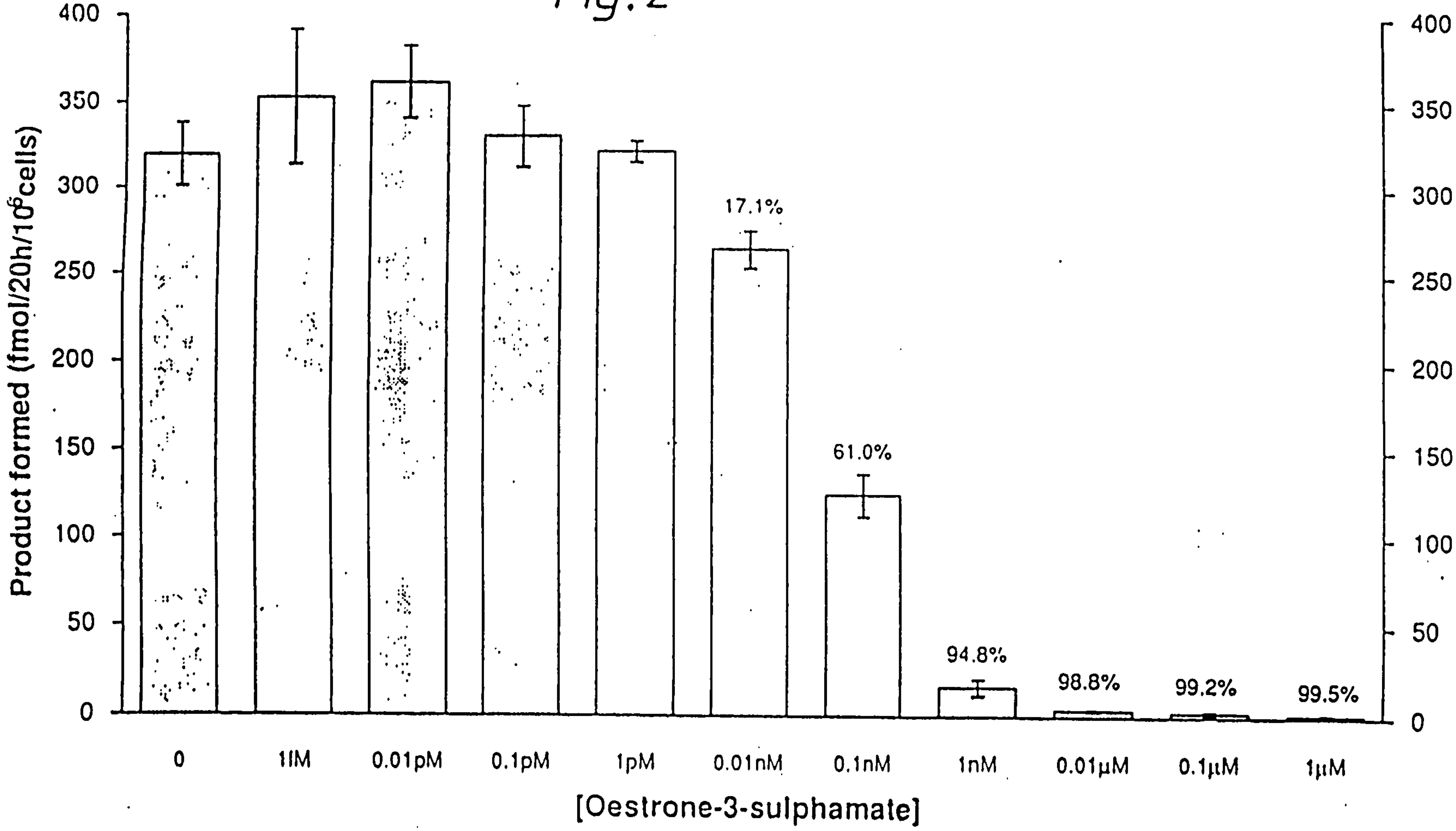

Product formed (fmol/20h/10⁶cells)
400
350
300
250
200
150
100
50
0
17.1%
61.0%
94.8%
98.8%
99.2%
99.5%
0
1lM
0.01pM
0.1pM
1pM
0.01nM
0.1nM
1nM
0.01μM
0.1μM
1μM
[Oestrone-3-sulphamate]

Fig. 3

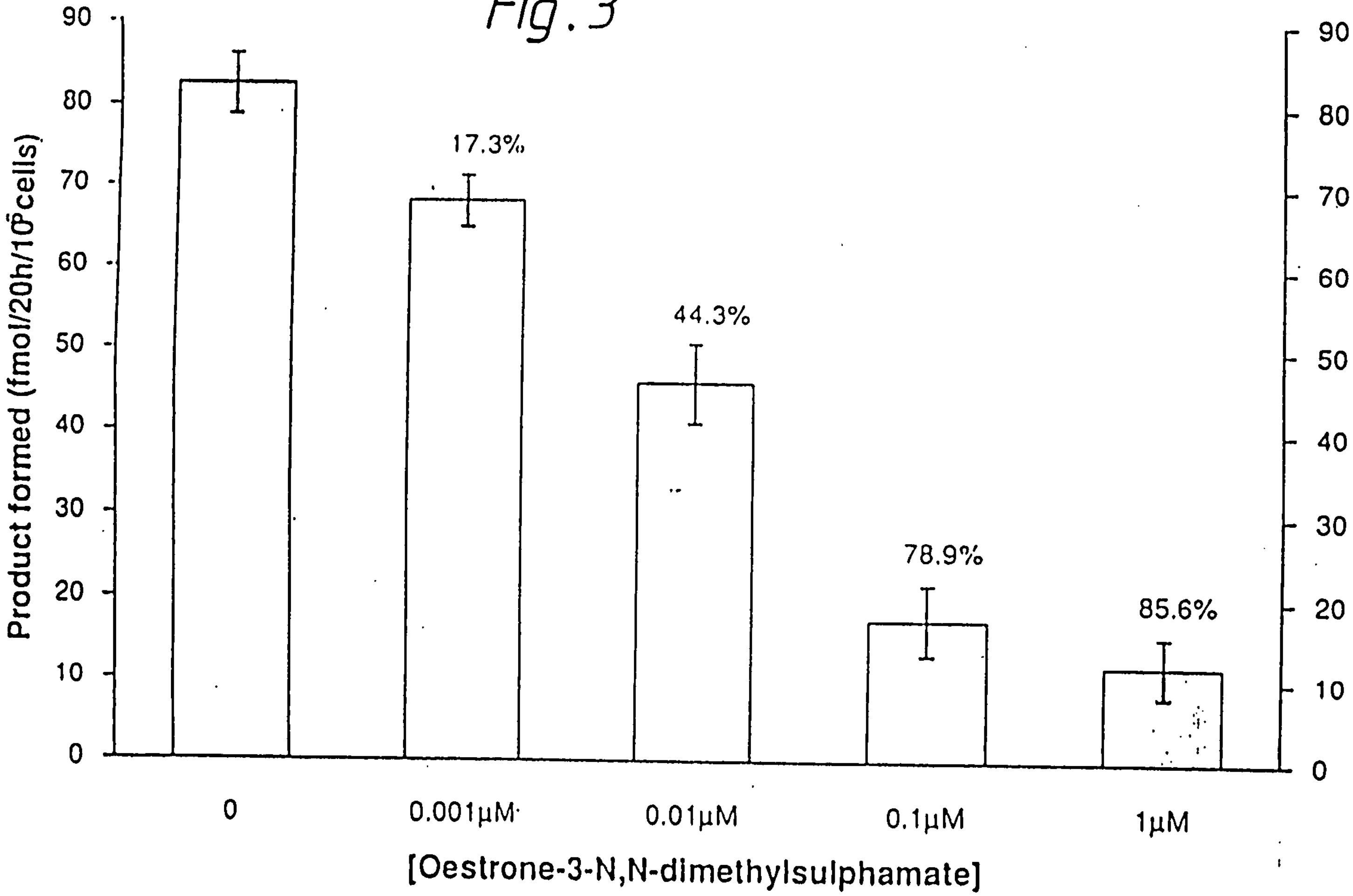

Product formed (fmol/20h/10⁶cells)
90
80
70
60
50
40
30
20
10
0
17.3%
44.3%
78.9%
85.6%
0
0.001μM
0.01μM
0.1μM
1μM
[Oestrone-3-N,N-dimethylsulphamate]

Fig. 4

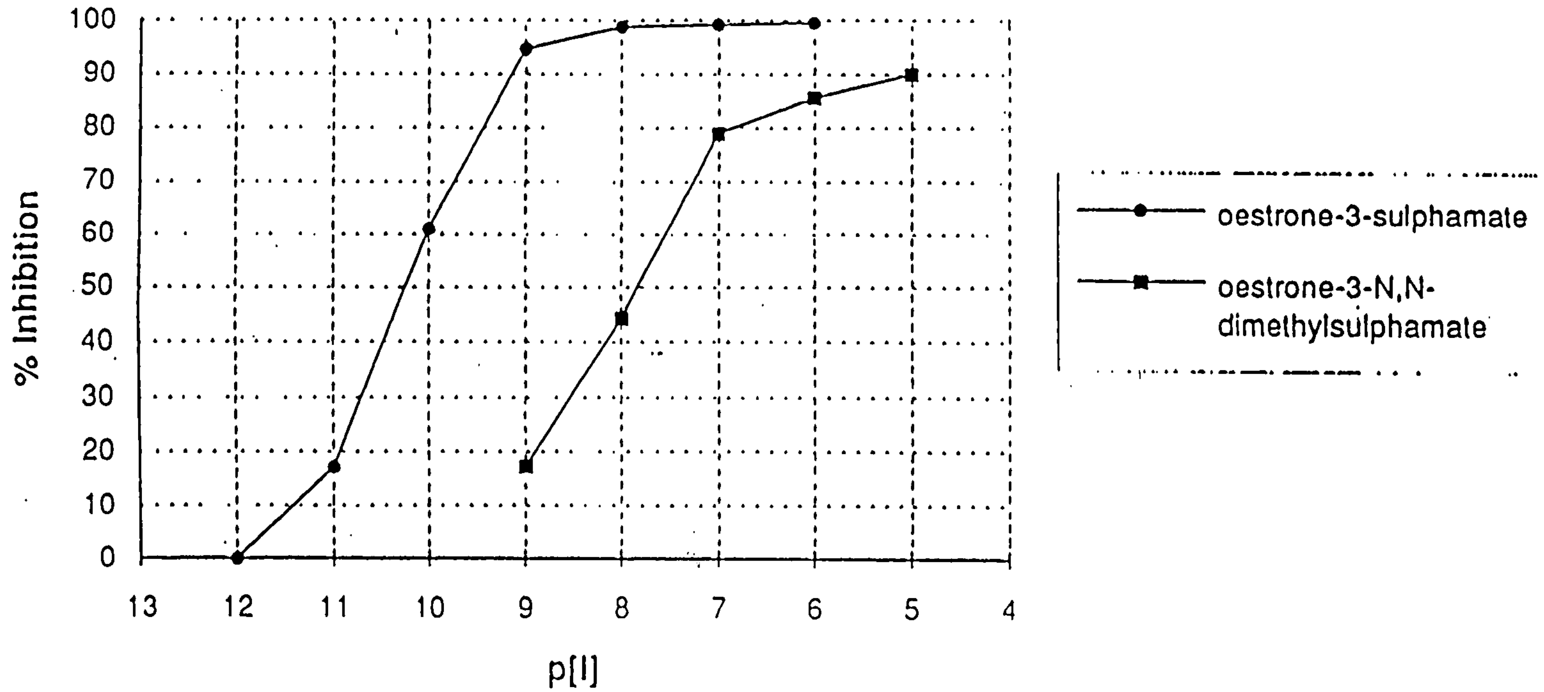
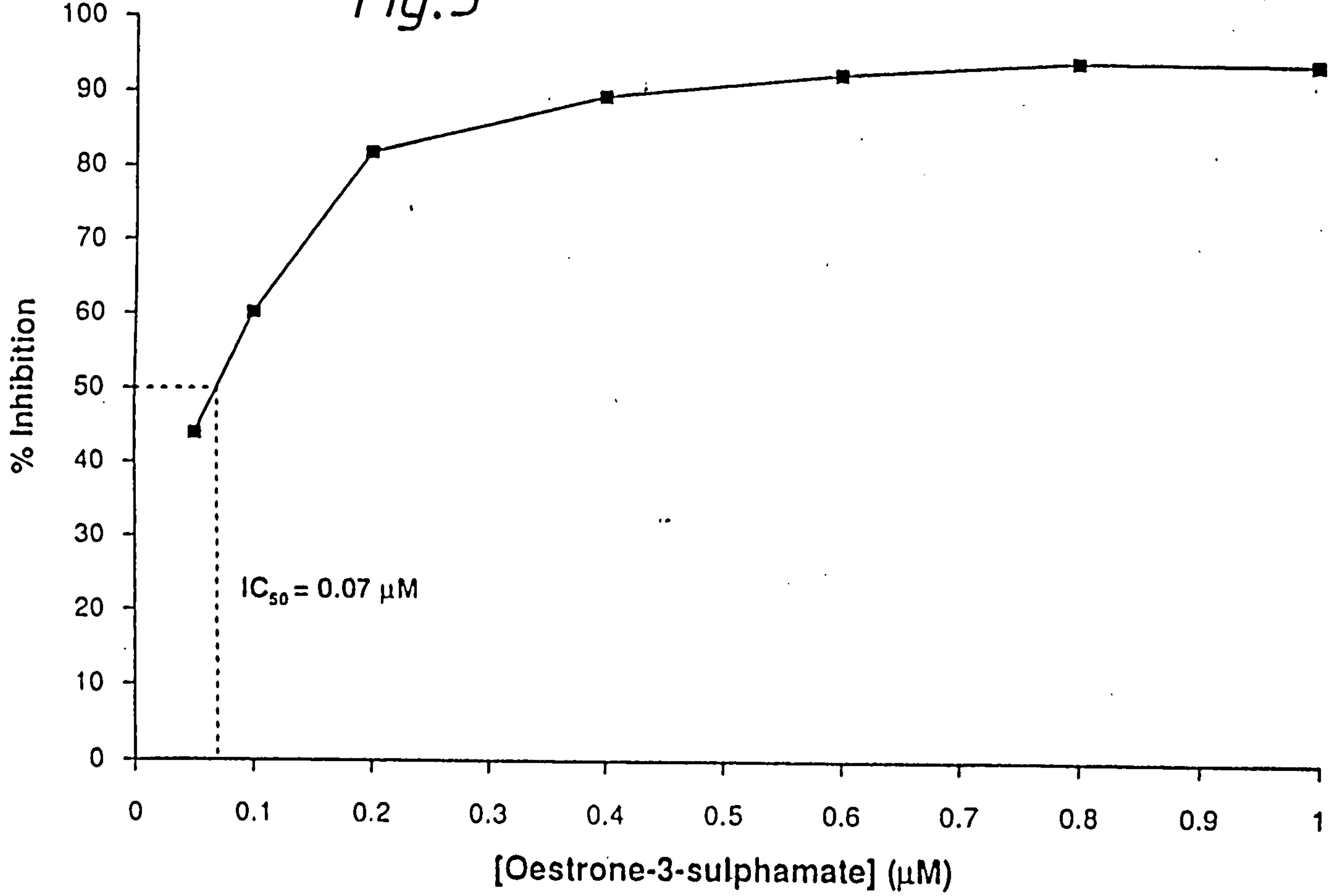
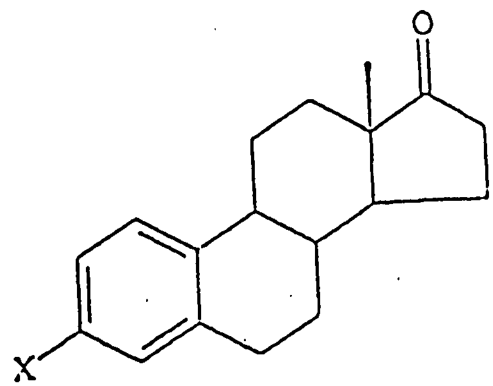

% Inhibition
100
90
80
70
60
50
40
30
20
10
0
13
12
11
10
9
8
7
6
5
4
p[I]
oestrone-3-sulphamate
oestrone-3-N,N-dimethylsulphamate

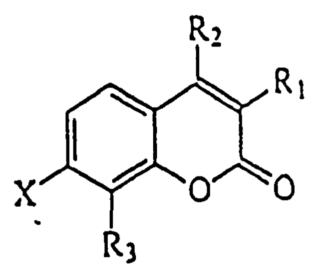
Fig.5


% Inhibition
100
90
80
70
60
50
40
30
20
10
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
IC_{50} = 0.07 μM
[Oestrone-3-sulphamate] (μM)



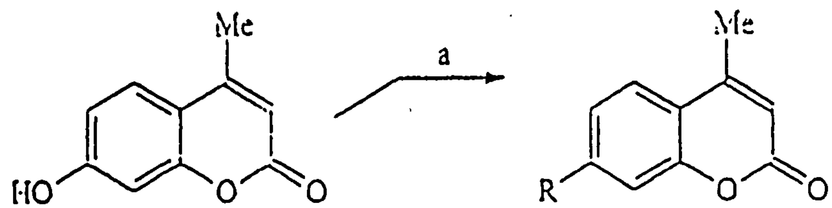
	X
(1)	-OH
(2)	$-OSO_3^-$
(3)	$-OSO_2NH_2$
(4)	$-NHSO_2NH_2$
(5)	$-SSO_2NH_2$

FIG. 6



	X	R_1	R_2	R_3
(11)	-OH	H	H	H
(12)	$-OSO_3^-$	H	CH_3	H
(13)	$-OSO_2NH_2$	H	H	H
(14)	$-OSO_2NH_2$	H	CH_3	H
(15)	$-OSO_2NH_2$	CH_3	CH_3	CH_3
(16)	$-OSO_2NH_2$	H	CF_3	H

FIG. 7



	R
(12)	$-OSO_3^-$
(14)	$-OSO_2NH_2$

FIG. 8

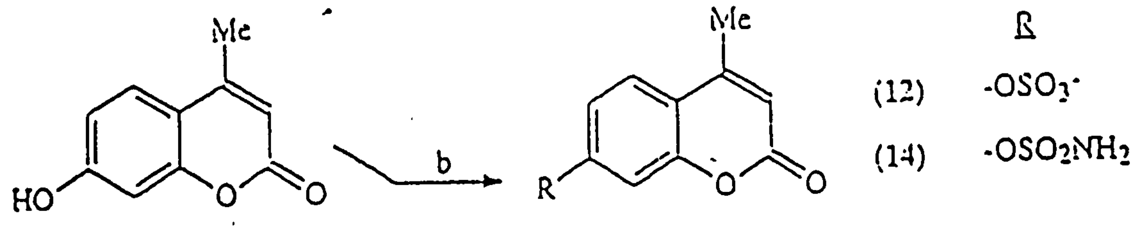


FIG. 9

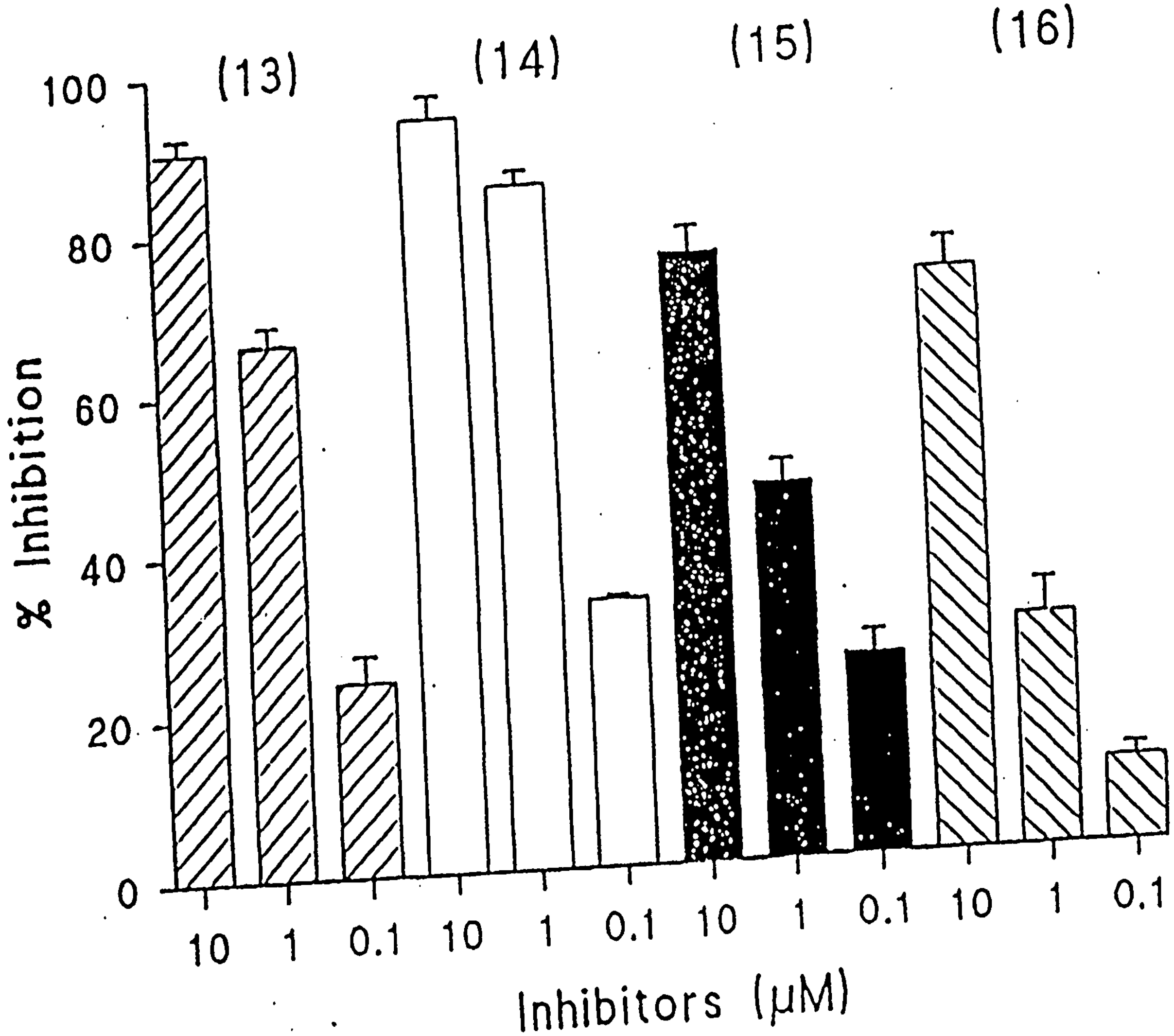
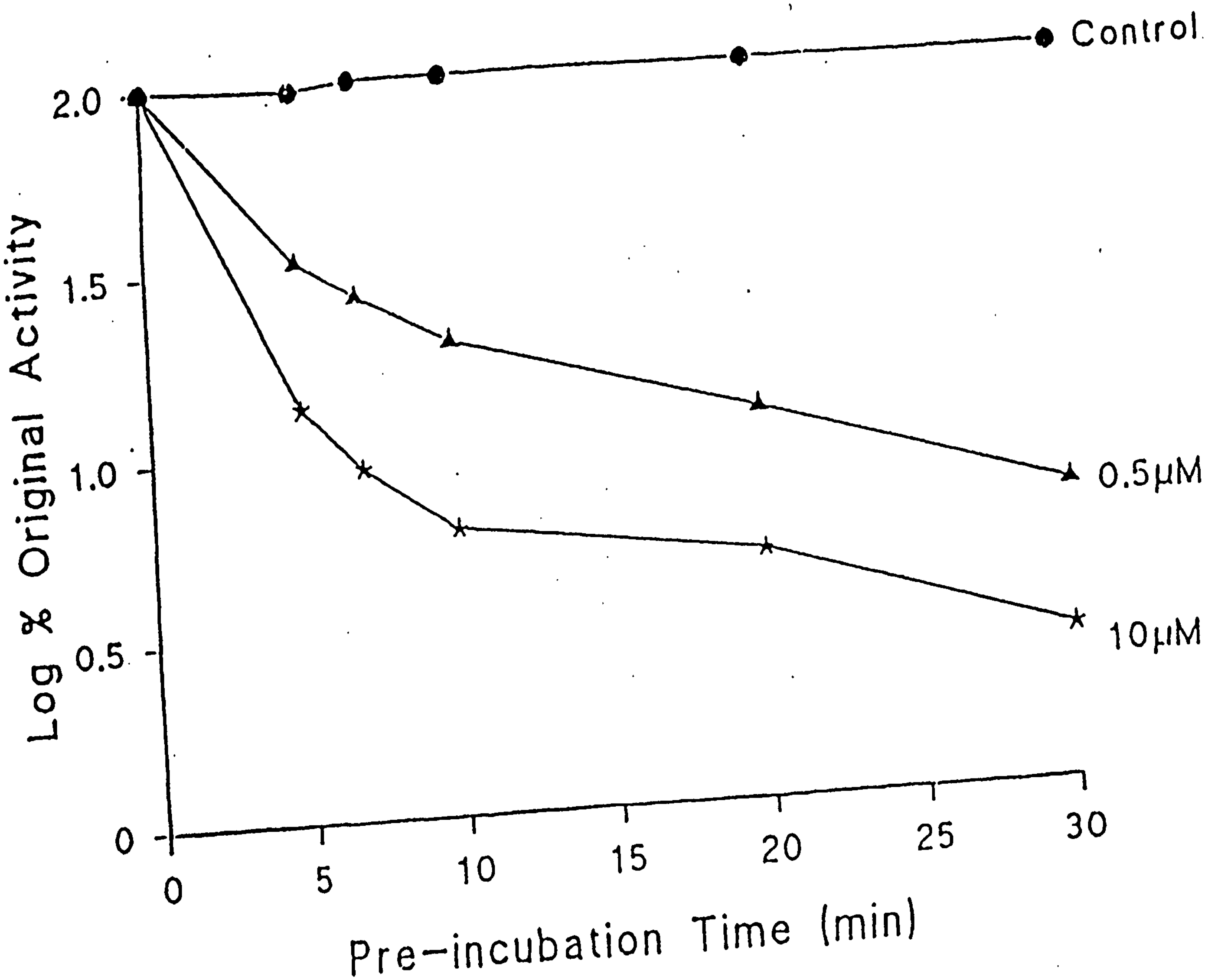

(13)
(14)
(15)
(16)
100
80
60
40
20
0
% Inhibition
10
1
0.1
10
1
0.1
10
1
0.1
10
1
0.1
Inhibitors (μM)

FIG. 10



Control
0.5μM
10μM
2.0
1.5
1.0
0.5
0
Log % Original Activity
0
5
10
15
20
25
30
Pre-incubation Time (min)

FIG. 11

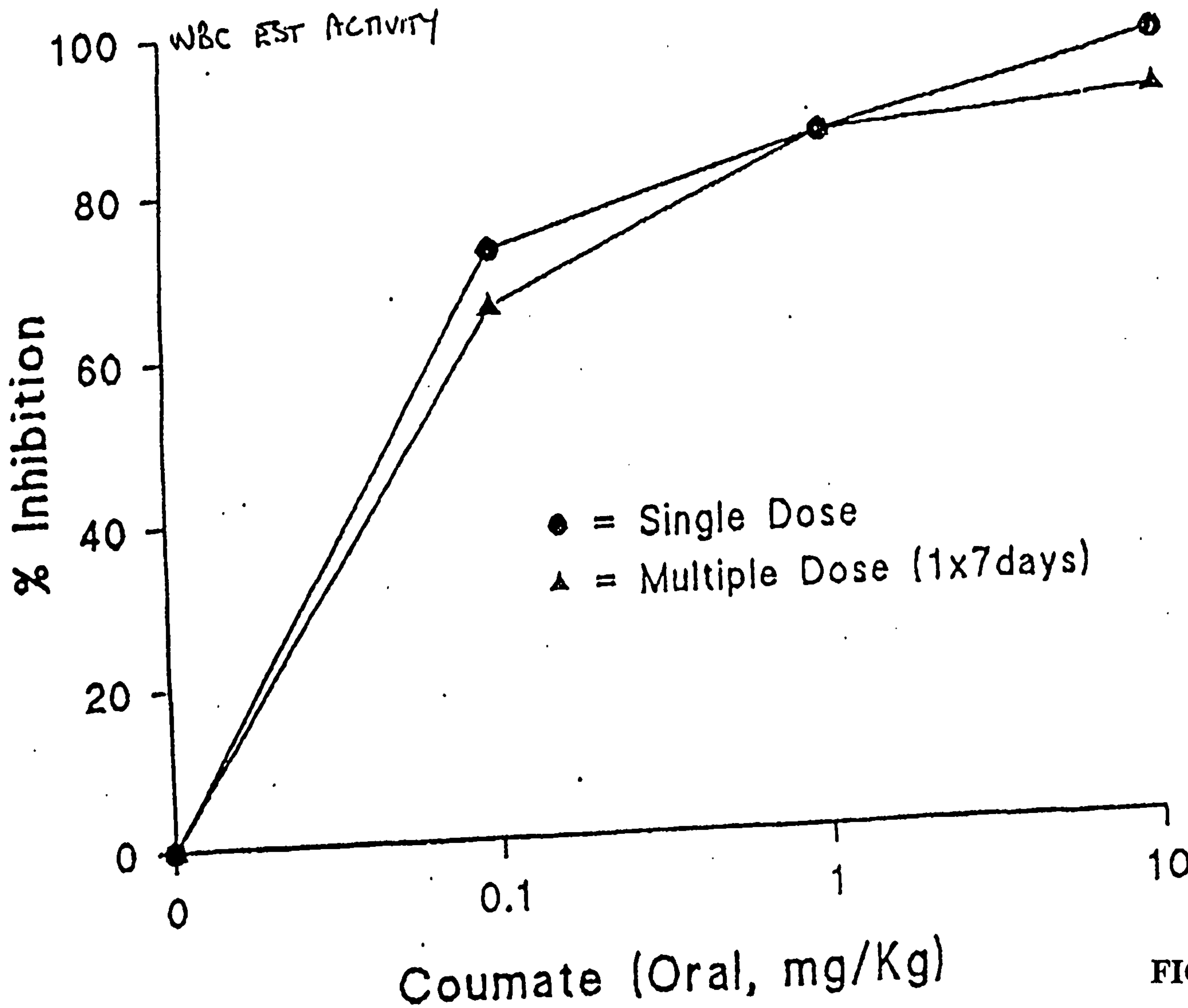
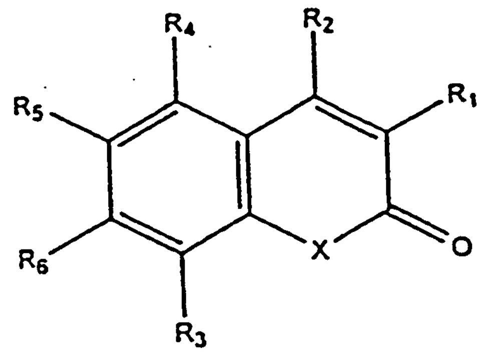
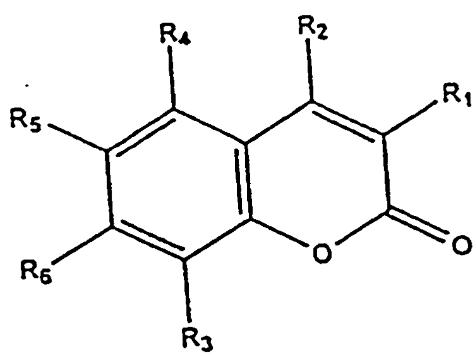

WBC EST ACTIVITY
100
80
60
40
20
0
% Inhibition
● = Single Dose
▲ = Multiple Dose (1x7days)
0
0.1
1
10
Coumate (Oral, mg/Kg)

FIG. 12

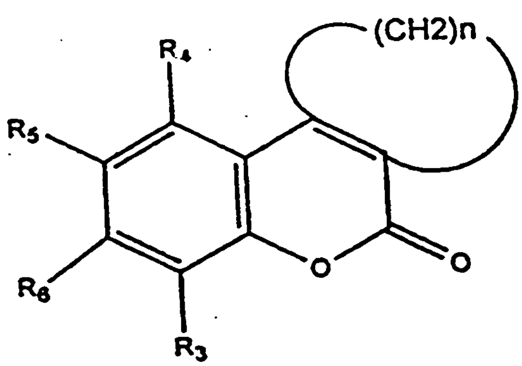
FIG. 13



(A)



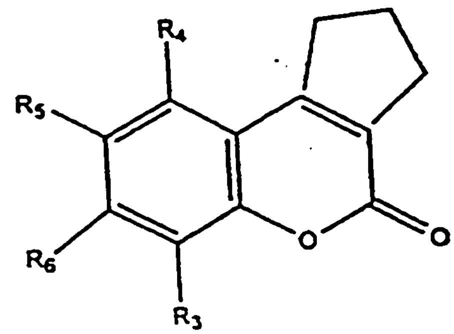
(B)



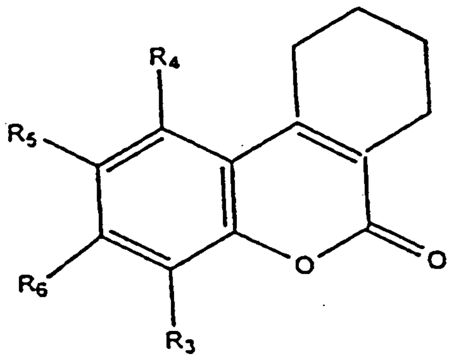
(C)

FIG. 14

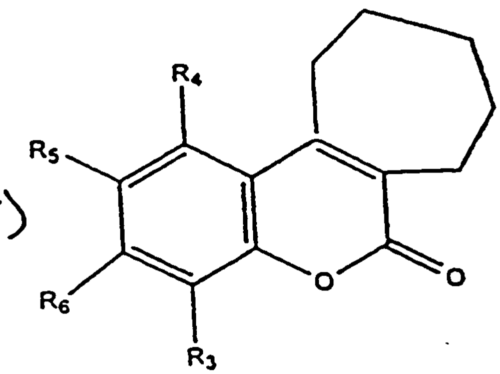
(D)


R_4
R_5
R_6
R_3
O
O

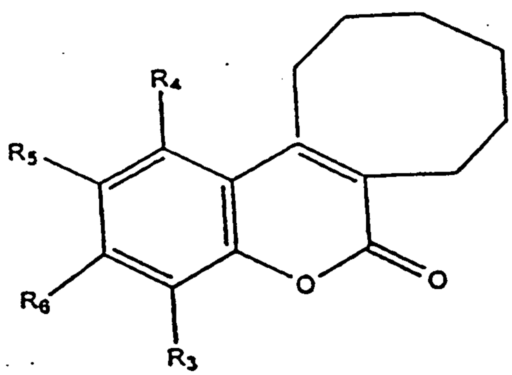
(E)


R_4
R_5
R_6
R_3
O
O

(F)


R_4
R_5
R_6
R_3
O
O

(G)


R_4
R_5
R_6
R_3
O
O

(H)

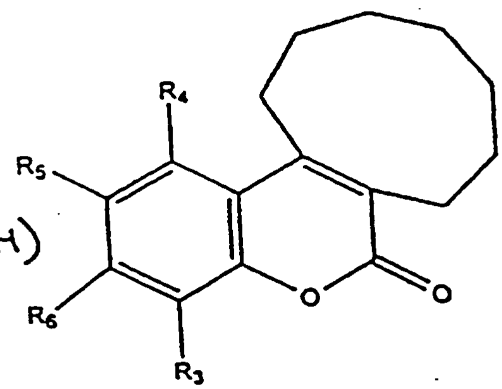
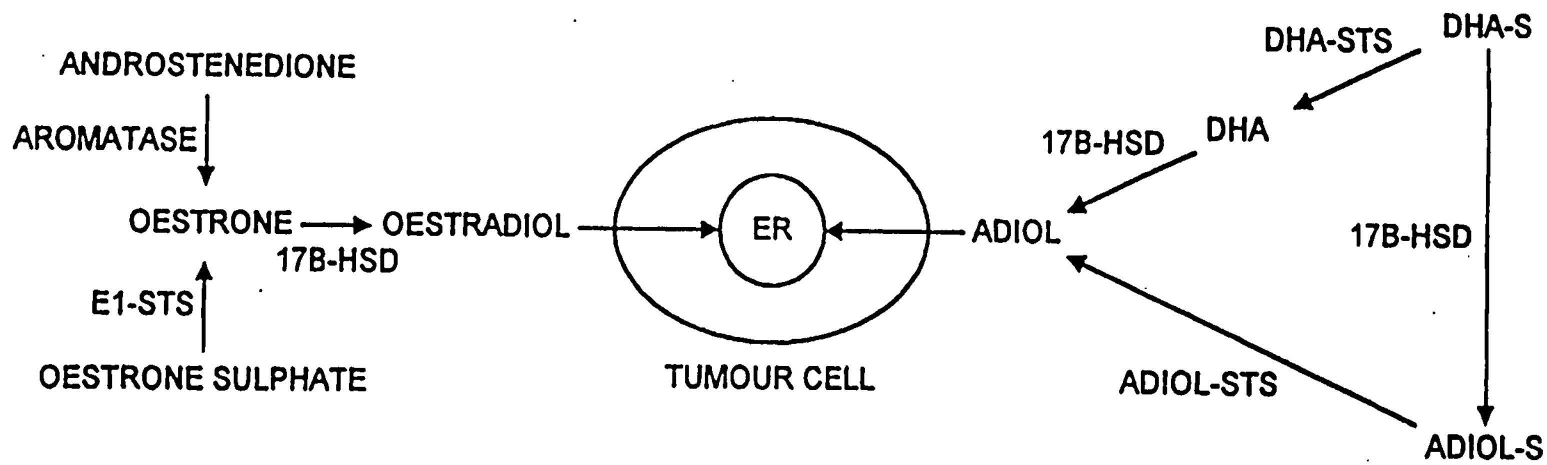

R_4
R_5
R_6
R_3
O
O

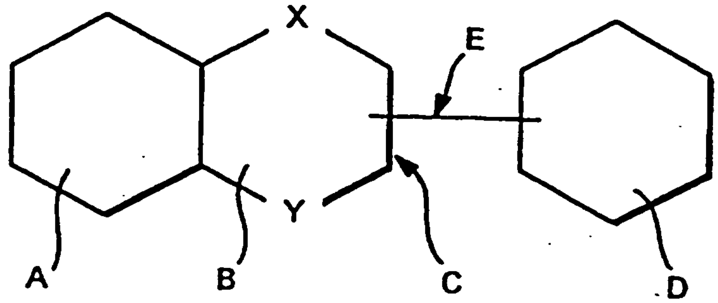
FIG. 15

ORIGIN OF OESTROGENIC STEROIDS IN POSTMENOPAUSAL WOMEN



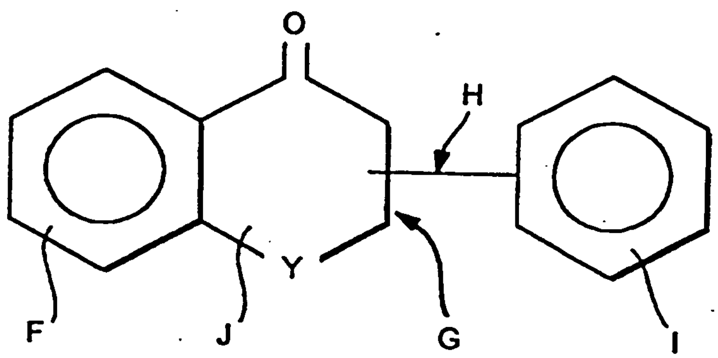
ER=OESTROGEN RECEPTOR, DHA / -S=DEHYDROEPIANDROSTERONE / -SULPHATE, ADIOL=ANDROSTENEDIOL, E1-STS=OESTRONE SULPHATASE, DHA -STS= DHA-SULPHATASE, ADIOL-STS=ADIOL SULPHATASE, 17B-HSD=OESTRADIOL 17B-HYDROXYSTEROID DEHYDROGENASE

FIG. 16a



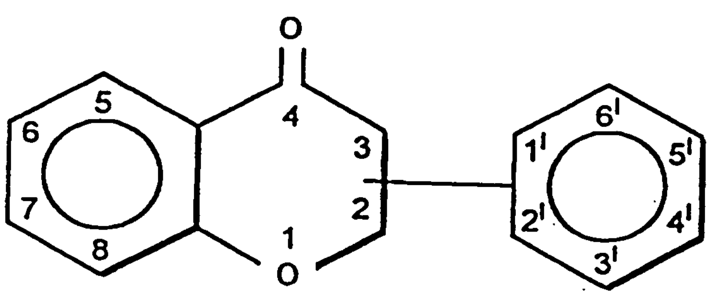
I

FIG. 16b



II

FIG. 16c



III

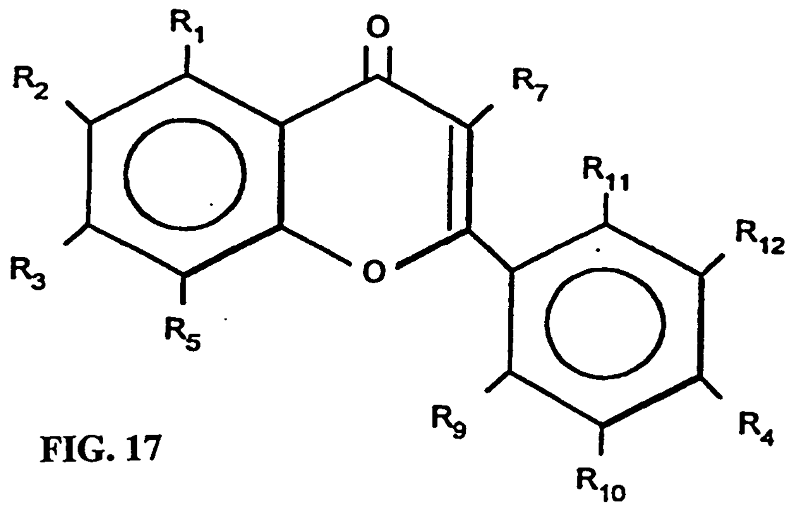
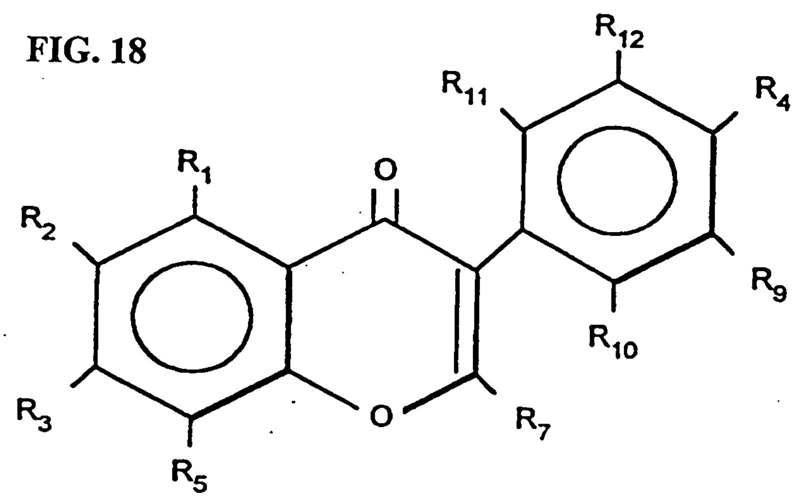


FIG. 17

IV

FIG. 18



V

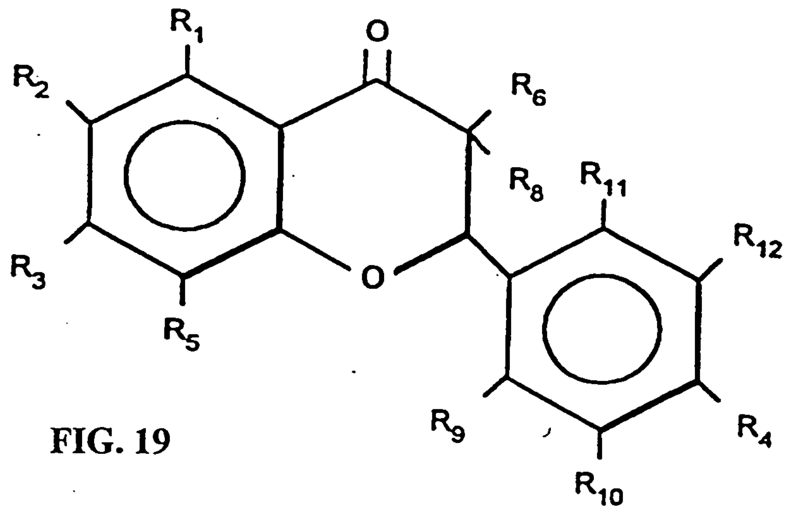
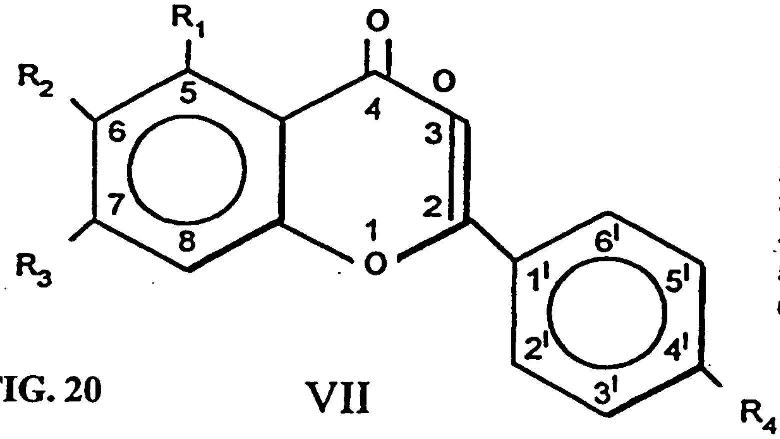


FIG. 19

VI

FLAVONES



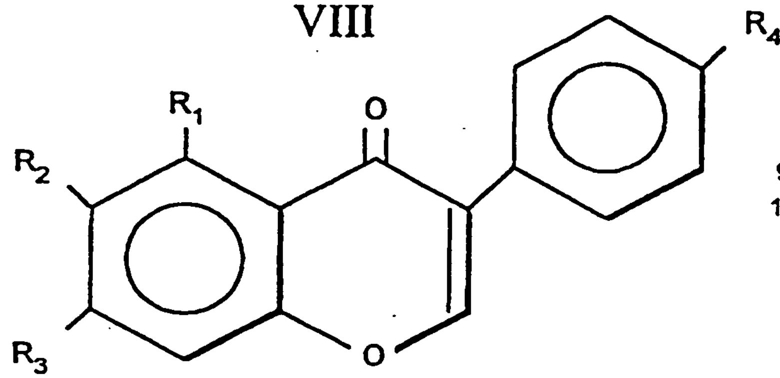
	R1	R2	R3	R4
1	H	OH	H	H
2	H	OSO_2NH_2	H	H
3	H	H	OH	H
4	H	H	OSO_2NH_2	H
5	OH	H	OH	H
6	OH	H	OSO_2NH_2	H

FIG. 20 VII

ISOFLAVONES

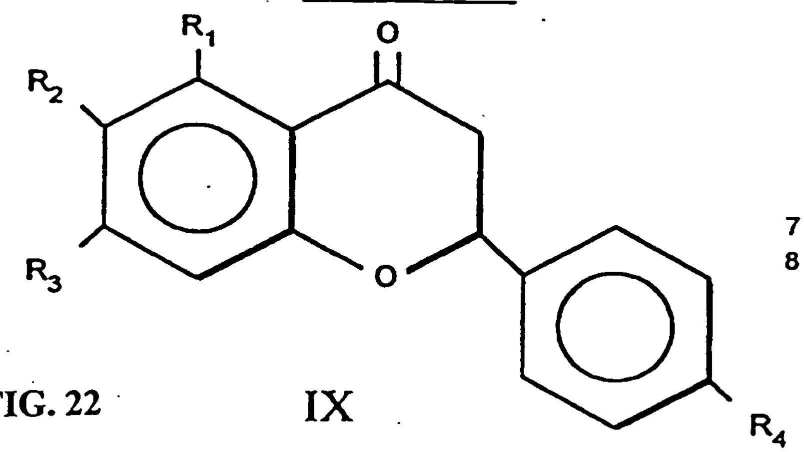
FIG. 21

VIII



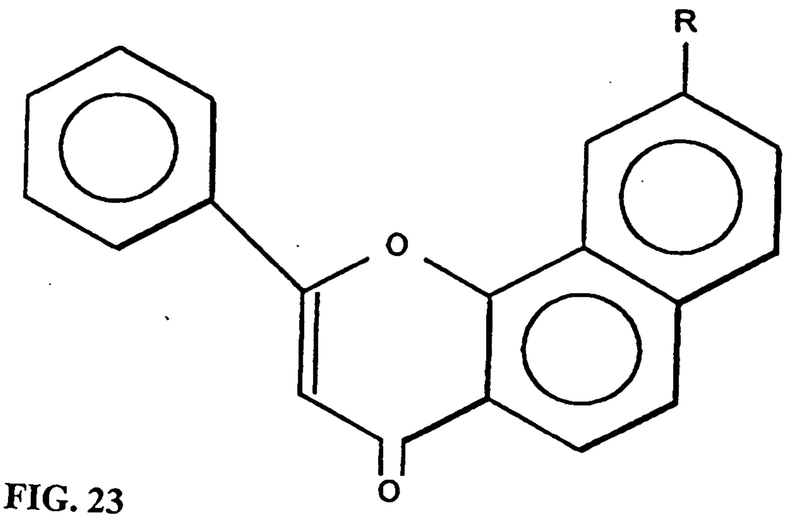
	R1	R2	R3	R4
9	OH	OH	H	OCH_3
10	OH	H	OSO_2NH_2	OCH_3

FLAVANONES



	R1	R2	R3	R4
7	OH	H	OH	OH
8	OH	H	OH	OSO_2NH_2

FIG. 22 IX



X

FIG. 23

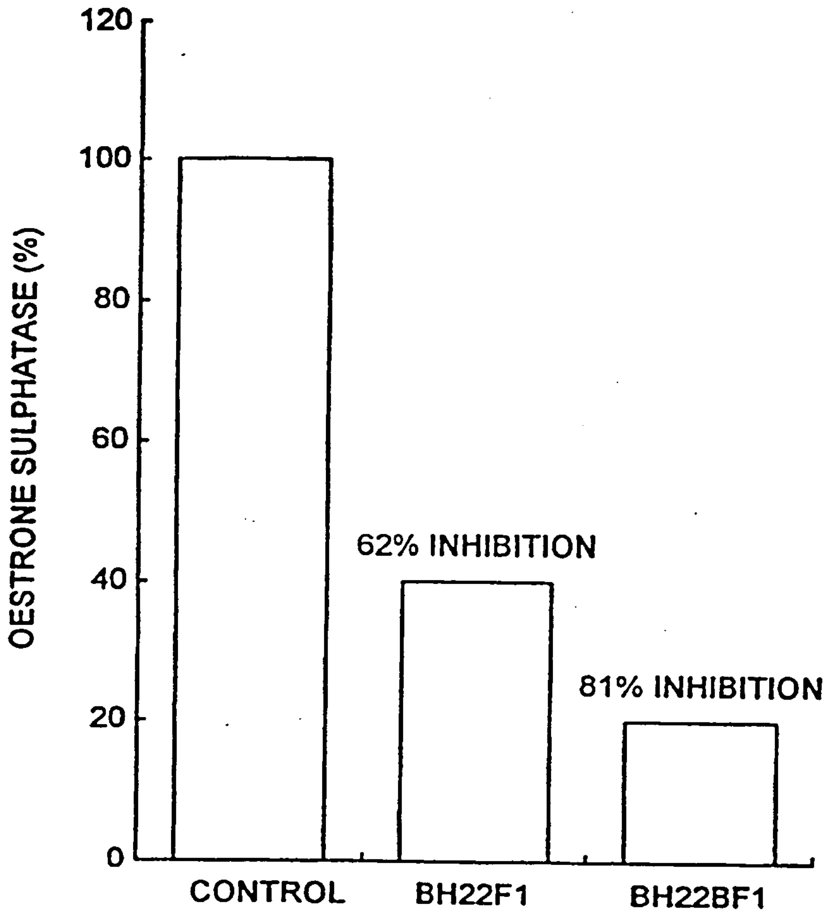
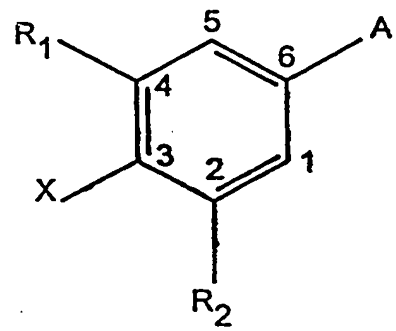

120
100
80
60
40
20
0
OESTRONE SULPHATASE (%)
62% INHIBITION
81% INHIBITION
CONTROL
BH22F1
BH22BF1

FIG. 24

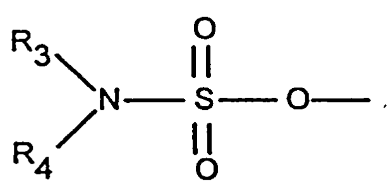
X - B - A   I

FIG. 25



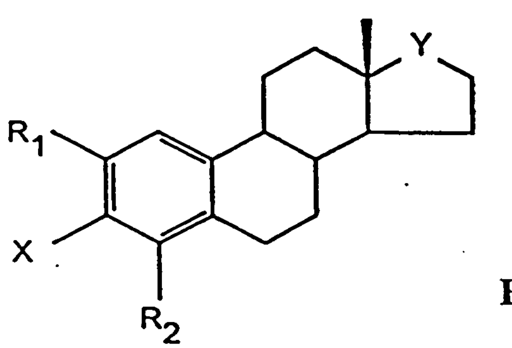
II

FIG. 26



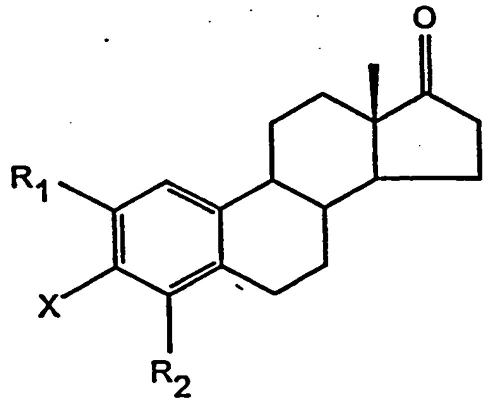
III

FIG. 27



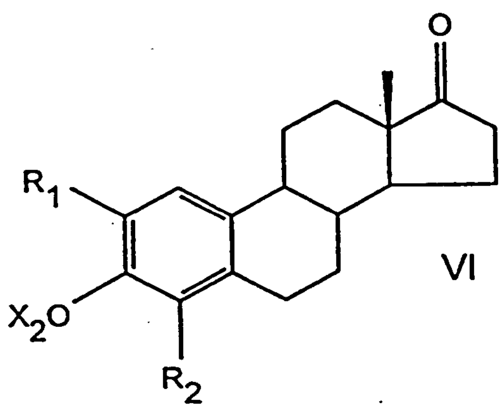
IV

FIG. 28



V

FIG. 29

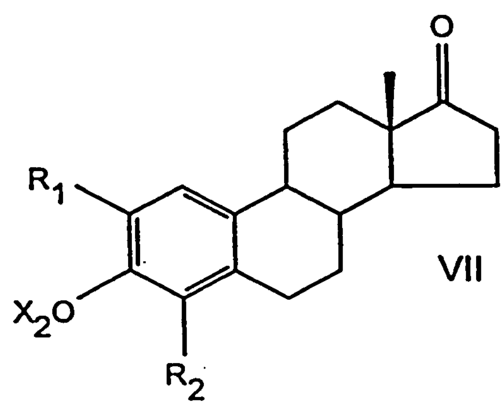


VI

X_2 = - SO_2NH_2

	R_1	R_2
a)	n-$CH_2CH_2CH_3$	H
b)	H	n-$CH_2CH_2CH_3$
c)	n-$CH_2CH_2CH_3$	n-$CH_2CH_2CH_3$

FIG. 30

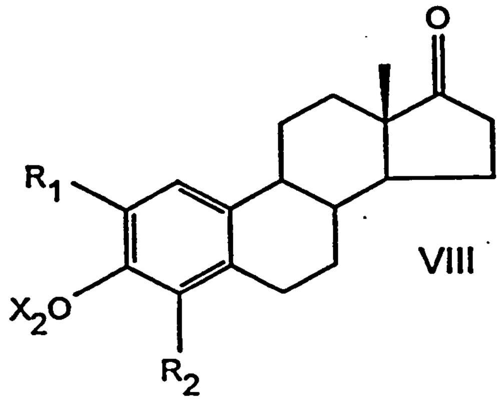


VII

X_2 = - SO_2NH_2

	R_1	R_2
a)	-$CH_2CH{=}CH_2$	H
b)	H	-$CH_2CH{=}CH_2$
c)	-$CH_2CH{=}CH_2$	-$CH_2CH{=}CH_2$

FIG. 31

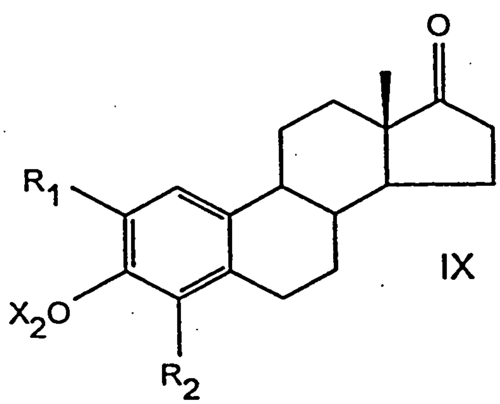


VIII

$X_2 = -SO_2NH_2$

	R_1	R_2
a)	H_3CO-	H
b)	H	H_3CO-
c)	H_3CO-	H_3CO-

FIG. 32

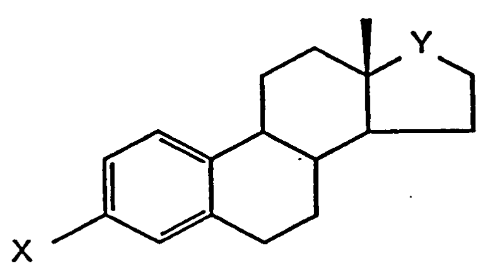


IX

$X_2 = -SO_2NH_2$

	R_1	R_2
a)	$-NO_2$	H
b)	H	$-NO_2$
c)	$-NO_2$	$-NO_2$

FIG. 33



X

FIG. 34

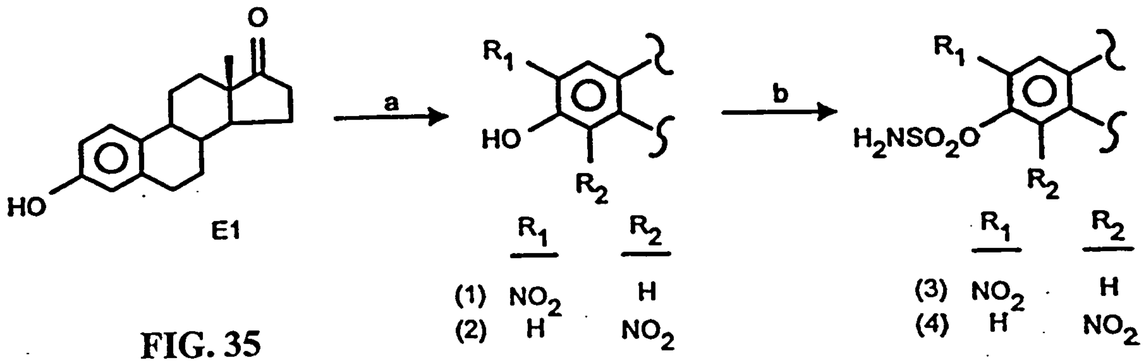


FIG. 35

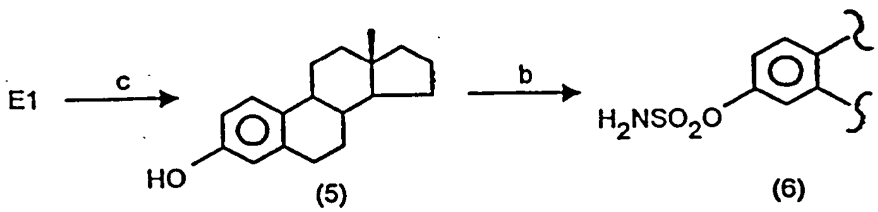


FIG. 36

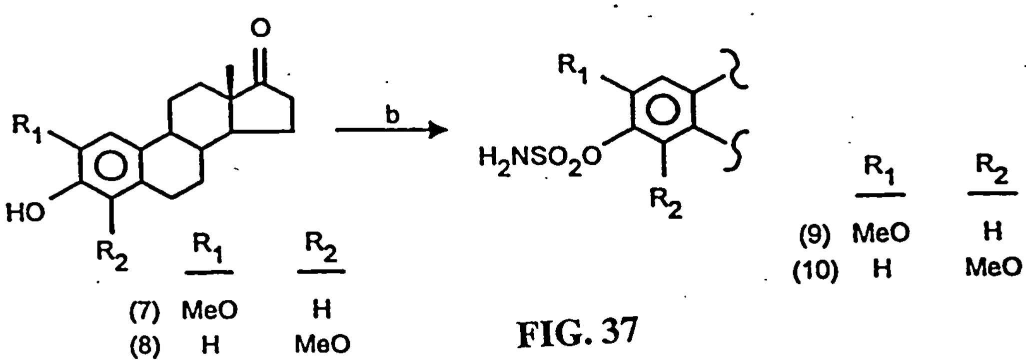
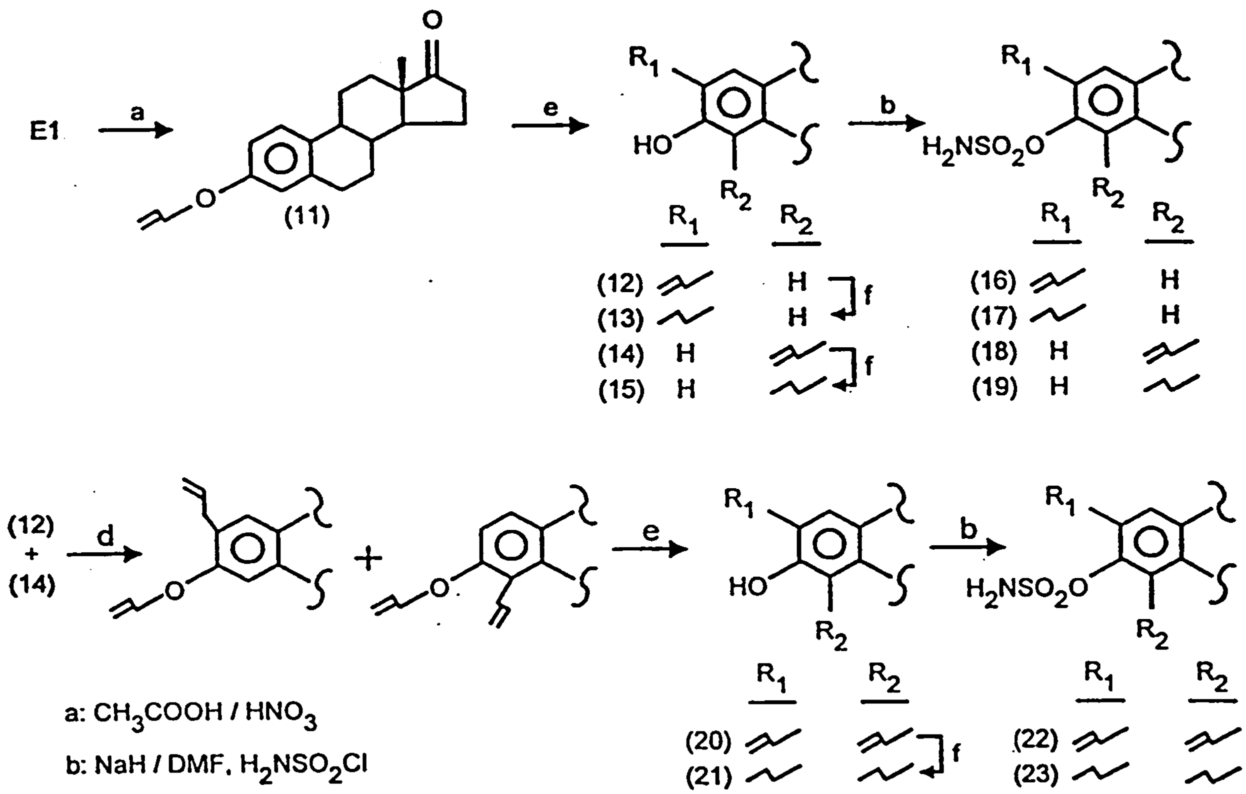


FIG. 37



a: CH_3COOH / HNO_3

b: NaH / DMF, H_2NSO_2Cl

c: $NH_2NH_2 \cdot H_2O$, KOH / DIETHYLENE GLYCOL

d: NaH / DMF, ⁄⁄ Br

e: N, N-DIETHYLANILINE, Δ

f: Pd/C, H_2

FIG. 38

IN VIVO INHIBITION OF OESTRONE SULPHATASE BY NOMATE (0.1 mg/Kg/DAY FOR 5 DAYS)

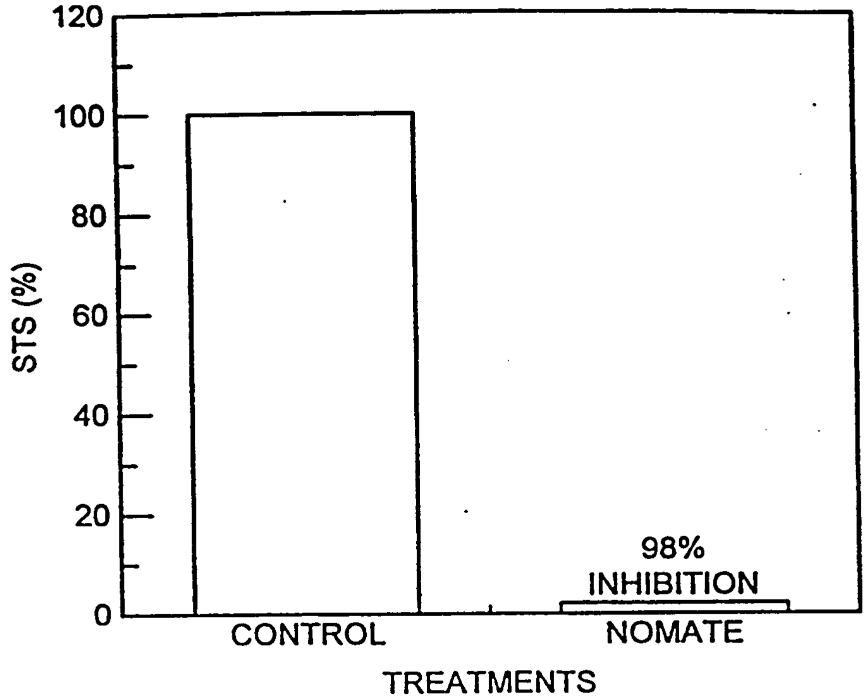


FIG. 39

LACK OF EFFECT OF NOMATE (0.1mg/Kg/DAY FOR 5 DAYS) ON UTERINE WEIGHTS OVARIECTOMISED RATS

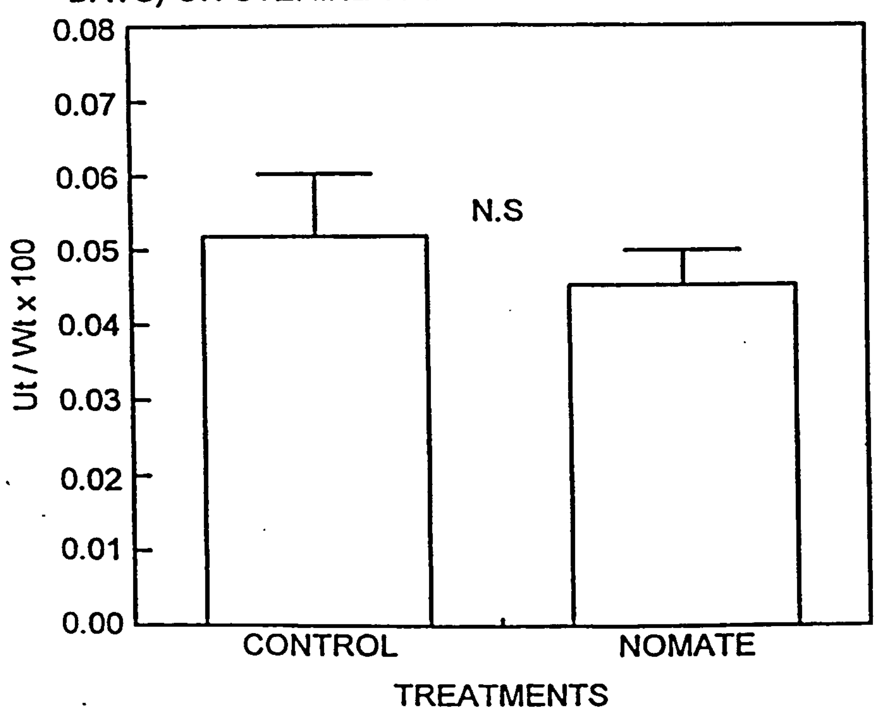


FIG. 40